Extreme Attributions Predict the Course of Bipolar Depression: Results From the STEP-BD Randomized Controlled Trial of Psychosocial Treatment

Jonathan P. Stange, MA; Louisa G. Sylvia, PhD; Pedro Vieira da Silva Magalhães, PhD; David J. Miklowitz, PhD; Michael W. Otto, PhD; Ellen Frank, PhD; Michael Berk, MD; Andrew A. Nierenberg, MD; and Thilo Deckersbach, PhD

ABSTRACT

Objective: Little is known about predictors of recovery from bipolar depression or moderators of treatment response. In the present study, we investigated attributional style (a cognitive pattern of explaining the causes of life events) as a predictor of recovery from episodes of bipolar depression and as a moderator of response to psychotherapy for bipolar depression.

Method: 106 depressed outpatients with *DSM-IV* bipolar I or II disorder who were enrolled in the Systematic Treatment Enhancement Program for Bipolar Disorder were randomly assigned to intensive psychotherapy for depression (n = 62) or to collaborative care (n = 44), a minimal psychoeducational intervention. The primary outcome was recovery status at each study visit as measured by the Clinical Monitoring Form. Attributional style was measured at baseline using the Attributional Style Questionnaire. Data were collected between 1998 and 2005.

Results: All analyses were by intention to treat. Extreme attributions predicted a lower likelihood of recovery ($P < .01$; OR = 0.93; 95% CI, 0.88–0.98) and longer time until recovery ($P < .01$; OR = 0.96; 95% CI, 0.93–0.99), independent of the effects of initial depression severity. Among individuals with more pessimistic attributional styles, higher initial depression severity predicted a lower likelihood of recovery ($P = .01$; OR = 0.64; 95% CI, 0.45–0.91) and longer time until recovery ($P < .001$; OR = 0.76; 95% CI, 0.66–0.88). There was no difference in recovery rates between intensive psychotherapy and collaborative care (OR = 0.90; 95% CI, 0.40–2.01) in the full sample.

Conclusions: These results suggest that extreme, rigid attributions may be associated with a more severe course of depression and that evaluating attributional style may help clinicians to identify patients who are at risk for experiencing a more severe course of depression.

Trial Registration: ClinicalTrials.gov identifier: NCT00012558

J Clin Psychiatry 2013;74(3):249–255

Submitted: *July 13, 2012; accepted November 12, 2012 (doi:10.4088/JCP.12m08019).*
Corresponding author: *Thilo Deckersbach, PhD, Department of Psychiatry, Bipolar Clinic and Research Program, Massachusetts General Hospital, 50 Staniford St, 5th Fl, Boston, MA 02114 (tdeckersbach@partners.org).*

Bipolar disorder is characterized by periods of depression and/or hypomania/mania, with lengthy periods of residual symptoms prior to recovery.[1] Individuals with bipolar disorder often experience a highly recurrent course of the disorder[2] with impairment in many areas, including cognitive impairment and poorer academic and work achievement.[3–10] People with bipolar disorder spend substantially more time depressed than being hypomanic or manic.[11] In particular, depressive symptoms account for much of the illness burden among individuals with bipolar disorder.[8,12,13]

Attributional style is a cognitive characteristic that has been useful for the understanding of the course of major depression in individuals with unipolar major depressive disorder.[14,15] Originally developed to apply learned helplessness theory to humans,[16] pessimistic attributional style is defined as the tendency to attribute the causes of negative events to internal, stable, and global reasons (eg, "I was fired because I am worthless") and to attribute the causes of positive events to external, unstable, and specific reasons (eg, "I received the promotion because I got lucky").[16] Research from several decades has indicated the utility of attributional style in identifying individuals at risk for developing unipolar depression.[14,15,17,18] In addition, several studies have found that extreme responses on measures of depressive cognition (eg, indicating "totally agree" or "totally disagree") predict relapse in unipolar depression.[19–21] In bipolar disorder, pessimistic attributional style has been found to predict increases in depressive symptoms,[22] particularly when vulnerable individuals experience life stressors.[23,24] However, it is unclear whether pessimistic attributional style is associated with longer depressive episodes in bipolar disorder, particularly after accounting for factors likely to be associated with recovery such as psychosocial treatment[25] and severity of initial depressive symptoms.

Pharmacotherapy is the first line of treatment for bipolar disorder, but pharmacologic treatments often fail to bring patients with bipolar disorder to sustained remission.[26,27] As a result, several adjunctive psychosocial interventions have been developed to treat bipolar disorder.[28,29] These include cognitive-behavioral therapies (CBT),[30–38] family-focused treatment (FFT),[39,40] and interpersonal and social rhythm therapy (IPSRT).[41,42] One of the largest randomized controlled treatment trials investigating the efficacy of psychotherapy for depression in bipolar disorder was conducted in the context of the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD).[25,43] This study found that FFT, IPSRT, and CBT were all equally effective in decreasing the length of time until recovery from depressive episodes and also improved functioning.[25,44]

Despite advances in psychotherapeutic and pharmacologic[28] treatment, many individuals with bipolar disorder recover slowly or not at all.[9,45–47] Researchers and clinicians have called for a better understanding of predictors of outcome of bipolar depression, as well as a better

Clinical Points

- Cognitive rigidity may be associated with a poorer course of depression in bipolar disorder, regardless of the valence of rigid thoughts.
- Pessimistic attributions and depression severity may work synergistically to maintain depression in bipolar disorder.
- Assessing attributional style may be clinically useful in identifying bipolar patients who are likely to have more severe courses of depression.

understanding of which individuals are likely to benefit from psychotherapy (ie, moderators of response to treatment).[28,48,49] For example, research has indicated that CBT may be more beneficial in patients with bipolar disorder who have fewer mood episodes,[38] whereas IPSRT and FFT may be superior for patients in more acutely ill states or individuals with a more severe course of the disorder.[28] Although it has been recognized that cognitive style may help identify which individuals may benefit most from psychotherapy,[28,50,51] to our knowledge, psychotherapy studies in bipolar disorder have not evaluated cognitive style as either a predictor for the duration of mood episodes or a moderator of treatment outcome.

This study evaluated the role of attributional style in predicting recovery from bipolar depression in the context of psychosocial treatment. Specifically, we evaluated the following questions: (1) Does attributional style (including extreme attributions) impact the duration of depressive episodes in bipolar disorder? More specifically, do bipolar patients with pessimistic attributional styles or who make extreme pessimistic attributions for life events take longer to recover from depression? (2) Is there an interaction between attributional style and initial depression severity? Specifically, do patients with pessimistic attributional style and high depression severity take longer to recover from depression? and (3) Does attributional style (including extreme attributions) moderate the efficacy of different types of psychotherapy for depression in bipolar disorder? To evaluate these questions, we used a sample of depressed bipolar patients who were enrolled in a randomized controlled trial of adjunctive psychotherapy for bipolar depression as part of STEP-BD.[25]

METHOD

Study Design and Participants

The 106 study participants (bipolar I [61%] or II [39%]) were drawn from 293 outpatients enrolled in the randomized controlled clinical trial[25] comparing the efficacy of psychotherapy and collaborative care treatment as part of STEP-BD (ClinicalTrials.gov identifier: NCT00012558). Data were collected between 1998 and 2005. STEP-BD is a National Institute of Mental Health–sponsored naturalistic multicenter study of the effectiveness of treatments for bipolar disorder[46] (for more details about the psychosocial treatment trial, see Miklowitz et al[25]). Inclusion criteria for the embedded randomized controlled psychotherapy trial included (1) being 18 years or older, (2) meeting *DSM-IV* criteria for bipolar I or II disorder and currently (during the prior 2 weeks) meeting criteria for a major depressive episode, (3) receiving current treatment with a mood stabilizer, (4) not currently undergoing psychotherapy or being willing to taper nonstudy psychotherapy sessions to 1 or fewer per month, (5) being able to speak English, and (6) being willing and able to give informed consent. Exclusion criteria were requiring immediate treatment for a *DSM-IV* substance or alcohol use or dependence disorder (excluding nicotine); being pregnant or planning pregnancy in the next year; having a history of intolerance, nonresponse, or contraindication to bupropion or paroxetine; or requiring dose changes in antipsychotic medications.[25] The STEP-BD trial was reviewed and approved by the human research institutional review boards of all participating universities.

The subsample of 106 patients from the larger STEP-BD trial had completed a measure of attributional style (the Attributional Style Questionnaire [ASQ][52]) prior to the first psychosocial treatment session (Table 1). This subsample did not differ from the original sample of 293 patients on any patient characteristics (χ^2 values < 2.15, t values < 1.23, P values > .14, Ns of 246–293), with the exceptions of the severity of initial depressive symptoms, which was higher in this subsample ($t = 9.18$, $P < .001$, N = 288), and Global Assessment of Functioning scores, which were lower in this subsample ($t = 7.84$, $P < .001$, N = 292).

Procedures and Outcomes

In STEP-BD, patients were diagnosed with bipolar disorder by study psychiatrists using the Affective Disorders Evaluation.[53,54] A second clinical interviewer verified the results using the Mini-International Neuropsychiatric Interview (version 5.0).[46,55] The 106 participants included in the present study were randomly assigned to an intensive psychotherapy (n = 62; CBT [n = 31], IPSRT [n = 20], or FFT [n = 11]) or to a collaborative care (n = 44) control condition (for more detailed information on these treatments, see Miklowitz et al,[25] Otto et al,[56] Miklowitz,[57] and Frank[58]). Collaborative care was a minimal psychosocial intervention that consisted of three 50-minute individual sessions conducted within 6 weeks after randomization and included psychoeducation about bipolar disorder and development of a relapse prevention contract. Collaborative care was intended to provide a brief version of the most common strategies shown to benefit patients with bipolar disorder.[57] All intensive psychosocial treatments consisted of up to 30 sessions lasting 50 minutes that were conducted by therapists who received training and supervision from nationally recognized experts in the specific intensive treatments.[25]

Measures

Clinical Monitoring Form. As in Miklowitz et al,[25] the primary outcome measure in the present study was patients' clinical recovery status, which was assessed at each visit via the Clinical Monitoring Form (CMF).[59] The CMF is a well-validated measure of the severity of *DSM-IV* mood

Table 1. Demographic and Illness Characteristics of 106 Bipolar Depressed Patients[a]

Variable	Value
Age, mean ± SD, y	39.68 ± 11.84
Female sex, %	62
Race, %	
Caucasian/white	94
African American/black	5
Asian/Pacific Islander	0
Other	1
Hispanic ethnicity, %	1
Education > 1 y of college, %	85
Annual income < $29,999, %	39
Marital status, %	
Married	34
Never married	37
Separated/divorced	28
Widowed	2
Diagnosis, %	
Bipolar I	61
Bipolar II	39
> 10 Previous depressive episodes, %	65
> 10 Previous manic episodes, %	67
Age at illness onset, mean ± SD, y	21.89 ± 10.09
Baseline depression symptoms, mean ± SD	6.23 ± 2.43
Baseline mania symptoms, mean ± SD	1.16 ± 1.17
Baseline GAF score, mean ± SD	55.91 ± 8.59
Medication, %	
Lithium	34
Atypical antipsychotic	26
Anticonvulsant	56
Benzodiazepine	25
Antidepressants	46
Stimulants	1
Valproate	36
Other mood stabilizers	28
Medication Load Index,[b] mean (SD)	3.64 (1.94)
Comorbid diagnoses, %	
Anxiety disorder (current)	49
Substance abuse/dependence (current)	13
ADHD (current)	14
Any lifetime comorbid disorder	83

[a]Percentages are not always based on 106 patients owing to missing data (see Miklowitz et al[25]).
[b]Coding system delineated by Phillips et al[61] was used.
Abbreviations: ADHD = attention-deficit/hyperactivity disorder, GAF = Global Assessment of Functioning.

symptoms and clinical status.[1,25,43,59,60] Clinical status (eg, recovered) is based on the presence or absence of *DSM-IV* criteria for episodes of depression or mania/hypomania, with recovered status defined as ≤ 2 moderate symptoms of depression for ≥ 8 of the previous weeks. Initial depression severity was defined as the CMF depressive symptom severity score (sum of the severity of all depression symptoms) at study entry and could range from 0 to 12. Initial medication types and dosages were also evaluated with the CMF. We also computed a variable representing psychiatric medication load, following the coding system delineated by Phillips et al,[61] such that higher values represent greater medication load (Table 1). Each psychiatric medication was coded as 1 or 2 depending on the therapeutic dosage.[61] Total medication load scores ranged from 0 to 8 (mean = 3.64, SD = 1.94).

Attributional Style Questionnaire. On the Attributional Style Questionnaire (ASQ),[52] participants rated the perceived cause of 6 hypothetical negative events and 6 hypothetical positive events using 7-point Likert scales in terms of internality ("due to me" vs "due to other people or circumstances"), stability ("will always be present" vs "will never be present"), and globality ("influences all situations in my life" vs "influences only this particular situation"). Scores were computed representing attributional style for negative events (mean = 86.39, median = 87, SD= 14.49; higher scores indicate more pessimistic attributional style) and positive events (mean = 84.85, median = 86, SD = 13.20; higher scores indicate more optimistic attributional style), and a difference score was computed, indicating the degree of optimistic versus pessimistic attributional styles, by subtracting the positive event score from the negative event score (mean = 1.54, median = 2, SD = 19.44; higher scores indicate more pessimistic attributional style). Scores on these subscales were comparable with previously published scores in healthy and depressed samples.[52,62]

Because of its utility in predicting recurrence of unipolar depression in previous research,[19–21] we also computed the number of "extreme" responses (rating of 1 or 7 on each item), resulting in variables for extreme pessimistic (mean = 5.84, median = 5, SD = 4.79), extreme optimistic (mean = 4.64, median = 3, SD = 4.80), and total extreme responses (mean = 10.48, median = 9, SD = 8.00), with higher scores indicating a greater frequency of extreme responses of each type. Internal consistency for the ASQ was high (α = .76).

Statistical Analysis

To evaluate the effects of attributional style and extreme responses on likelihood of recovery and time until recovery, we conducted logistic regressions and Cox proportional hazards models, respectively. All analyses were by intention to treat. Patients were included until their final assessment point with a maximum of 365 days in the study[25] (mean = 291.78 days, SD = 96.51). The proportionality of risk assumption was upheld for all survival analyses. Odds ratios less than 1 indicate lower likelihood of recovery and greater time until recovery.

To evaluate the incremental ability of attributional style and extreme responses to predict recovery status beyond the effects of treatment or initial depressive symptoms, treatment condition (collaborative care or intensive psychotherapy) and initial depressive symptoms were included in step 1 of the regression models, and ASQ variables were included in step 2. Prior to evaluating ASQ variables as moderators of treatment effects, we determined whether there were significant effects of treatment condition on likelihood of recovery and time until recovery.[63]

RESULTS

Incremental Effects of Attributional Style on Recovery from Depression

Demographic and clinical characteristics of the present sample are shown in Table 1 (for the characteristics of the full sample, see Miklowitz et al[25]). The results of the primary analyses (logistic regression models using attribution scores, psychosocial treatment condition, and initial depression severity to predict recovery and Cox regression analyses to

Table 2. Logistic Regression and Cox Regression Analyses Evaluating Attributional Style and Extreme Responses as Predictors of Likelihood of Recovery and Time Until Recovery From Depression[a,b]

Step and Predictor	*B*	Wald	OR	*P*	95% CI	Δ R^2
ASQ total score models						
Logistic regression: predicting recovery						
1 CMF depressive symptoms	−0.14	2.47	0.87	.12	0.730–1.035	.04
Treatment group[c]	0.02	< 0.01	1.02	.96	0.447–2.332	
2 ASQ total	> −0.01	0.09	< 1.00	.76	0.976–1.018	< .01
Cox regression: predicting time until recovery						
1 CMF depressive symptoms	−0.12	5.92	0.89	.02	0.812–0.978	
Treatment group[c]	0.05	0.04	1.05	.84	0.647–1.714	
2 ASQ total	< 0.01	0.01	1.00	.94	0.988–1.011	< .01
ASQ extreme total models						
Logistic regression: predicting recovery						
1 CMF depressive symptoms	−0.16	3.16	0.85	.08	0.715–1.017	.04
Treatment group[c]	0.10	0.05	1.10	.82	0.470–2.597	
2 ASQ extreme total	−0.07	6.70	0.93	< .01	0.883–0.983	.09
Cox regression: predicting time until recovery						
1 CMF depressive symptoms	−0.13	6.87	0.88	.01	0.794–0.967	
Treatment group[c]	−0.02	0.01	0.98	.92	0.596–1.599	
2 ASQ extreme total	−0.05	6.86	0.96	< .01	0.925–0.989	.07
Models for interaction between ASQ total score and initial depressive symptoms						
Logistic regression: predicting recovery						
1 Treatment group[c]	−0.07	0.02	0.94	.88	0.401–2.187	< .01
2 CMF depressive symptoms	−0.19	3.59	0.83	.06	0.679–1.007	.04
ASQ total	> −0.01	0.04	1.00	.84	0.975–1.020	
3 CMF depressive symptoms × ASQ total	−0.01	3.81	0.99	.05	0.981–0.999	.06
Cox regression: predicting time until recovery						
1 Treatment group[c]	0.02	< 0.01	1.02	.95	0.621–1.659	
2 CMF depressive symptoms	−0.14	8.40	0.87	< .01	0.794–0.956	.03
ASQ total	0.02	2.99	1.02	.84	0.997–1.045	
3 CMF depressive symptoms × ASQ total	> −0.01	4.06	0.99	.04	0.993–0.999	.04
Models for interaction between ASQ extreme total and initial depressive symptoms						
Logistic regression: predicting recovery						
1 Treatment group[c]	0.08	0.03	1.08	.86	0.456–2.549	< .01
2 CMF depressive symptoms	−0.13	1.91	0.88	.17	0.725–1.057	.12
ASQ extreme total	−0.08	6.83	0.93	.01	0.876–0.981	
3 CMF depressive symptoms × ASQ extreme total	−0.01	0.60	0.99	.44	0.972–1.012	.01
Cox regression: predicting time until recovery						
1 Treatment group[c]	−0.03	0.01	0.97	.92	0.595–1.594	
2 CMF depressive symptoms	−0.13	6.14	0.88	.01	0.799–0.974	.09
ASQ extreme total	−0.05	7.16	0.95	.01	0.919–0.987	
3 CMF depressive symptoms × ASQ extreme total	> −0.01	0.56	1.00	.46	0.986–1.006	.01

[a]N = 106.
[b]Change in R^2 for logistic regressions represents Nagelkerke R^2 change since previous step, an estimate of the increment in variance in the probability of recovery accounted for by the predictors tested since the previous step.[76] Change in R^2 for Cox regressions represents Cox-Snell R^2 change since previous step, an estimate of the relative association between survival and the predictors tested since the previous step.[76]
[c]Treatment group = intensive psychosocial treatment (1) vs collaborative care (0).
Abbreviations: ASQ = Attributional Style Questionnaire, CMF = Clinical Monitoring Form.

predict time to recovery) are in Table 2. All analyses had a total sample of 106 participants. The severity of initial depressive symptoms was not associated with likelihood of recovery (Wald = 2.64, OR = 0.87; 95% CI, 0.73–1.03; $P = .10$; $R^2 = 0.04$), but it was associated with longer time to recovery (Wald = 6.57; OR = 0.89; 95% CI, 0.81–0.97; $P = .01$). Higher medication load predicted a lower likelihood of recovery (Wald = 4.38; OR = 0.80; 95% CI, 0.64–0.99; $P = .04$, $R^2 = 0.06$) and a greater time to recovery (Wald = 11.37; OR = 0.80; 95% CI, 0.70–0.91; $P < .001$). ASQ variables were not significantly associated with initial depressive symptoms (r values < 0.13, P values > .19) or medication load (r values ≤ 0.16, P values > .10).

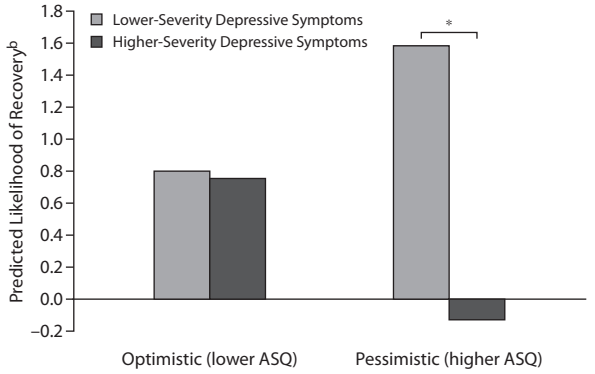
Controlling for treatment group (intensive psychotherapy and collaborative care) and initial depressive symptoms, there was no significant effect of ASQ total score on likelihood of recovery or time until recovery (Table 2). However, consistent with our hypotheses, more ASQ total extreme responses were associated with a significantly lower likelihood of recovery and a longer time until recovery (Table 2). This effect was significant for extreme pessimistic responses (logistic $P = .02$, Cox $P = .04$) as well as extreme optimistic responses (logistic $P = .04$, Cox $P = .03$).

Patients' ASQ total scores interacted with initial depressive symptoms in predicting likelihood of recovery and time until recovery (Table 2, Figure 1). To probe the nature of these interactions, we centered the ASQ variables and tested the effects of depressive symptoms on recovery at 1 standard deviation above or below the ASQ means.[64] Consistent with the hypothesis that initial depressive symptoms had a greater impact on course of depression among individuals with a negative attributional style, more severe initial depressive symptoms were associated with lower likelihood of recovery (Wald = 6.25; OR = 0.64; 95% CI, 0.45–0.91; $P = .01$) and greater time until recovery (Wald = 14.56; OR = 0.76; 95% CI, 0.66–0.88; $P < .001$) among individuals with more pessimistic attributional styles, but did not predict likelihood of recovery (Wald = 0.38; OR = 1.09; 95% CI, 0.83–1.42; $P = .54$) or time until recovery (Wald = 0.04; OR = 0.99; 95% CI, 0.87–1.13; $P = .85$) among individuals with more optimistic attributional styles.

Effects of Treatment on Recovery From Depression

In contrast with the full sample of 293 patients (see Miklowitz et al[25]), there was no significant effect of treatment group in this study's subsample (N = 106) on likelihood of recovery from depression ($B = -0.11$; Wald = 0.07; OR = 0.90; $P = .79$; 95% CI, 0.40–2.01; $R^2 < 0.01$) or time to recovery ($B = -0.10$; Wald = 0.16; OR = 0.91; $P = .69$; 95% CI, 0.56–1.47). Per Kraemer et al,[63] this precluded the investigation of whether attributional style moderated the effect of psychotherapy compared to collaborative care on recovery.

Figure 1. Interaction Between Attributional Style and Initial Depressive Symptoms Predicting Likelihood of Recovery From Depression[a]



[a]Effects of initial depressive symptoms are plotted at +/– 1 standard deviation from the mean of ASQ scores.
[b]0 = 0%, 1 = 100% predicted likelihood of recovery.
*$P < .05$.
Abbreviation: ASQ = Attributional Style Questionnaire.

All results remained consistent after controlling for study site, number of psychosocial treatment sessions, bipolar I or II status, age, gender, education, number of lifetime episodes of depression and mania/hypomania, baseline manic symptoms, psychiatric medication load, and age at onset of bipolar disorder.

DISCUSSION

Our results indicated that, among depressed patients with bipolar I or II disorder, extreme pessimistic and extreme optimistic responses predicted a lower likelihood of recovery and a greater time until recovery from depression. These results remained significant when initial depression severity, psychosocial treatment type, and symptoms of mania were included in regression models. We had hypothesized this effect for pessimistic responses; yet, the emergence of significant prediction for extreme optimistic responses suggests that it is not simply the negative nature of extreme thoughts that may be important for prediction of recovery in bipolar depression, but the fixity or rigidity of thought, as reflected by greater belief in both positive and negative extreme thoughts.

Cognitive rigidity, typically assessed with neuropsychological tasks, has itself been linked to both disorder onset and a more chronic course of depression.[65–67] In contrast, being more fluidly aware of the possible inaccuracies of thoughts (metacognitive awareness) is associated with lower relapse into depression.[68] Our results are in accord with both of these findings and suggest that the presence of extreme cognitions (regardless of valence) may indicate a lower likelihood of recovery from depression in bipolar disorder.

The tendency to make extreme attributions about the causes of life events appears to be associated with a more severe course of bipolar depression. To recover, these individuals may need to overcome not only their depressed mood but also the extreme, rigid thought style through which they interpret negative events in their lives, which may serve to maintain depressed mood. Indeed, individuals with a pessimistic attributional style and more severe initial depressive symptoms experienced the worst course of depression, suggesting that the combination of these factors may be associated with a poorer prognosis. These results are consistent with studies that report that a pessimistic attributional style is a risk factor for depressed mood among individuals with bipolar disorder.[23,24] The present study indicates that pessimistic attributional style, and particularly extreme attributions, may also predict the course of bipolar depression by means of maintaining depressed mood. Thus, evaluating attributional style among patients presenting for treatment for bipolar depression may allow for adaptation of treatments in order to address these issues. For example, it is possible that bipolar individuals who make extreme attributions would benefit from cognitive restructuring using hypothetical scenarios to help them make more balanced attributions or from observing their attributions using a mindful, nonjudgmental, decentered approach to their thoughts, as suggested by mindfulness-based treatments for bipolar disorder.[69–71]

To our knowledge, this study is the first to evaluate cognitive style as a predictor of the course of bipolar depression. We utilized a sample of patients who were early in the development of a major depressive episode and thus may be representative of patients with bipolar disorder who are seen for acute care in clinical practice.[25] Nevertheless, several limitations of the study should be noted. First, only a subsample of participants from the full trial of psychosocial treatments for bipolar depression completed the ASQ, so it is unclear whether these results would extend to the full sample in STEP-BD. In this subsample, intensive psychotherapy was not associated with a more rapid time to recovery from depression, possibly because patients in the subsample had more severe initial depressive symptoms and poorer functioning than those in the full sample.[25] Second, attributional style was evaluated only at the time of randomization, so it was not possible to evaluate whether attributional style changed as a result of treatment condition or in concert with recovery from depression. Third, although our primary outcome measure of recovery from the depressive episode is clinically relevant, other ways of evaluating course of illness (eg, continued residual mood symptoms, switch to mania, or symptom worsening[49]) should be evaluated in greater detail in the future.

Fourth, we did not evaluate intervening life events as suggested by vulnerability-stress models of bipolar disorder.[23,24,72] Evaluating life stress in combination with cognitive vulnerabilities such as attributional style might allow clinicians to predict more precisely which patients are likely to have more severe courses of illness.[51] In addition, our sample was relatively homogeneous in terms of race and socioeconomic status. Finally, the primary findings were characterized by small to medium effect sizes. Nonetheless, even small effects may be clinically relevant in the evaluation of predictors of recovery from bipolar depression.[73]

In conclusion, attributional style and extreme attributions for life events may be important predictors of the course of

bipolar depression. Future research should examine whether evaluating attributions in the context of life stress,[23,24,72] as well as attributions for actual (as opposed to hypothetical) negative life events,[74] allows for better prediction of which individuals take longer to recover from bipolar depression. Finally, more work is needed to determine whether enhancing psychotherapies such as CBT by more deliberately targeting negative or rigid cognitions, or by using cognitive remediation strategies for treating cognitive rigidity,[75] would improve the course of depression among bipolar individuals undergoing pharmacologic treatment.

Drug names: bupropion (Wellbutrin, Aplenzin, and others), lithium (Lithobid and others), paroxetine (Paxil, Pexeva, and others).

Author affiliations: Department of Psychology, Temple University, Philadelphia, Pennsylvania (Mr Stange); Department of Psychiatry, Massachusetts General Hospital and Harvard Medical School, Boston (Drs Sylvia, Nierenberg, and Deckersbach); National Institute for Translational Medicine, Hospital de Clínicas de Porto Alegre, Universidade Federal do Rio Grande do Sul, Porto Alegre, Brazil (Dr Magalhães); Division of Child and Adolescent Psychiatry, UCLA School of Medicine, Los Angeles (Dr Miklowitz); Department of Psychology, Boston University, Boston, Massachusetts (Dr Otto); Department of Psychiatry, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania (Dr Frank); and School of Medicine, Deakin University, Geelong, Australia; Orygen Youth Health Research Centre, Centre of Youth Mental Health, Florey Institute for Neuroscience and Mental Health, and Department of Psychiatry, University of Melbourne, Parkville, Australia (Dr Berk).

Potential conflicts of interest: **Dr Sylvia** has been a consultant for Bracket Global and Clintara, has received research support from National Institute of Mental Health (NIMH), is a former stockholder in Concordant Rater Systems, and has received other financial or material support from New Harbinger Publishers. **Dr Miklowitz** has received research support or honoraria from NIMH, Brain and Behavior Research Foundation, Danny Alberts Foundation, and Attias Family Foundation and has received other financial or material support from Guilford Press and John Wiley and Sons. **Dr Otto** has been a consultant for MicroTransponder. **Dr Frank** has been a consultant for Servier and has received other financial or material support from Guilford Press and the American Psychological Association Press. **Dr Berk** is an employee of Barwon Health, Deakin University; has received research support from National Institutes of Health, National Health and Medical Research Council, and CRC Simons; has received honoraria from Lundbeck, AstraZeneca, Servier, Eli Lilly, and ISBD Korea; has been on the speakers/advisory boards of AstraZeneca, Lundbeck, Eli Lilly, and Janssen; and has received other financial or material support from Allen & Unwin and Cambridge University Press. **Dr Nierenberg** has received honoraria or travel expenses from American Society of Clinical Psychopharmacology, Australasian Society for Bipolar Disorder, Bayamon Region Psychiatric Society (San Juan, Puerto Rico), Belvoir Publishing, Boston Center for the Arts, Corcept, CRICO, Dartmouth, Dey, LP/Mylan, Israel Society for Biological Psychiatry, Johns Hopkins University, National Association of Continuing Education, PAI, Pamlab, Physicians Postgraduate Press, Ridge Diagnostics, Slack Publishing, Sunovion, Teva, University of Florida, University of Michigan, University of New Mexico, University of Miami, University of Wisconsin, and Wolters Kluwer Publishing; has received potential consulting honoraria from AstraZeneca, Bristol-Myers Squibb, Forest, Pfizer, and Ridge Diagnostics; and has received potential support of research at MGH through Biogen Idec, Dey, Pamlab, Shire, and Sunovion. He owns stock options in Appliance Computing, Inc (MindSite.com) and Brain Cells, Inc. Additional income is possible from Infomedic.com depending on overall revenues of the company, but no revenue has been received to date. Through MGH, Dr Nierenberg is named for copyrights to the Clinical Positive Affect Scale and the MGH Structured Clinical Interview for the Montgomery-Asberg Depression Rating Scale exclusively licensed to the MGH Clinical Trials Network and Institute. **Dr Deckersbach** has received funding for his research from National Alliance for Research on Schizophrenia and Depression, Tourette Syndrome Association, Obsessive-Compulsive Foundation, and Tufts University; has received honoraria, consultation fees, and/or royalties from the MGH Psychiatry Academy, BrainCells Inc, Systems Research and Applications Corporation, Boston University, Catalan Agency for Health Technology Assessment and Research, National Association of Social Workers Massachusetts, Massachusetts Medical Society, Tufts University, National Institute on Drug Abuse, and Oxford University Press; and has participated in research funded by National Institutes of Health, National Institute on Aging, Agency for Healthcare Research and Quality, Janssen, Forest, Shire, Medtronic, Cyberonics, and Northstar. **Mr Stange** and **Dr Magalhães** report no relevant financial interests.

Funding/support: STEP-BD was funded in part by contract N01MH80001 from the National Institute of Mental Health (Gary S. Sachs, MD). Support for the development of the psychosocial treatments was provided by grants MH29618 (Dr Frank), MH43931 (Dr Miklowitz), and MH55101 (Dr Miklowitz) from the National Institute of Mental Health and by National Alliance for Research on Schizophrenia and Depression (Dr Miklowitz). Mr Stange was supported by National Research Service Award F31MH099761 from the National Institute of Mental Health. Dr Deckersbach was supported in part by a K-23 NIMH Career Award 1K23MH074895-01A2.

REFERENCES

1. Perlis RH, Ostacher MJ, Patel JK, et al. Predictors of recurrence in bipolar disorder: primary outcomes from the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD). *Am J Psychiatry*. 2006;163(2):217–224.
2. Goldberg JF, Burdick KE, eds. *Cognitive Dysfunction in Bipolar Disorder*. Washington, DC: American Psychiatric Publishing; 2008.
3. Murray CJL, Lopez AD. *The Global Burden of Disease: A Comprehensive Assessment of Mortality and Disability From Diseases, Injuries, and Risk Factors in 1990 and Projected to 2020*. Boston, MA: Harvard University Press; 1996.
4. Martínez-Arán A, Vieta E, Colom F, et al. Cognitive impairment in euthymic bipolar patients: implications for clinical and functional outcome. *Bipolar Disord*. 2004;6(3):224–232.
5. Grant BF, Stinson FS, Dawson DA, et al. Prevalence and co-occurrence of substance use disorders and independent mood and anxiety disorders: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Arch Gen Psychiatry*. 2004;61(8):807–816.
6. Angst F, Stassen HH, Clayton PJ, et al. Mortality of patients with mood disorders: follow-up over 34–38 years. *J Affect Disord*. 2002;68(2-3):167–181.
7. Nusslock R, Abramson LY, Harmon-Jones E, et al. A goal-striving life event and the onset of bipolar episodes: perspective from the behavioral approach system (BAS) dysregulation theory. *J Abnorm Psychol*. 2007;116(1):105–115.
8. Kessler RC, Akiskal HS, Ames M, et al. Prevalence and effects of mood disorders on work performance in a nationally representative sample of US workers. *Am J Psychiatry*. 2006;163(9):1561–1568.
9. Goodwin FK, Jamison KR. *Manic-Depressive Illness*. New York, NY: Oxford University Press; 1990.
10. Keck PE Jr, McElroy SL, Strakowski SM, et al. Factors associated with pharmacologic noncompliance in patients with mania. *J Clin Psychiatry*. 1996;57(7):292–297.
11. De Dios C, Ezquiaga E, Garcia A, et al. Time spent with symptoms in a cohort of bipolar disorder outpatients in Spain: a prospective, 18-month follow-up study. *J Affect Disord*. 2010;125(1–3):74–81.
12. Rosa AR, Reinares M, Michalak EE, et al. Functional impairment and disability across mood states in bipolar disorder. *Value Health*. 2010;13(8):984–988.
13. Baldessarini RJ, Salvatore P, Khalsa HM, et al. Morbidity in 303 first-episode bipolar I disorder patients. *Bipolar Disord*. 2010;12(3):264–270.
14. Alloy LB, Abramson LY, Keyser J, et al. Negative cognitive style. In: Dobson KS, Dozois DJA, eds. *Risk Factors in Depression*. New York, NY: Academic Press; 2008:237–262.
15. Abela JRZ, Auerbach RP, Seligman MEP. Dispositional pessimism across the lifespan. In: Dobson KS, Dozois DJA, eds. *Risk Factors in Depression*. New York, NY: Academic Press; 2008:195–220.
16. Abramson LY, Seligman ME, Teasdale JD. Learned helplessness in humans: critique and reformulation. *J Abnorm Psychol*. 1978;87(1):49–74.
17. Alloy LB, Abramson LY, Whitehouse WG, et al. Prospective incidence of first onsets and recurrences of depression in individuals at high and low cognitive risk for depression. *J Abnorm Psychol*. 2006;115(1):145–156.
18. Sweeney PD, Anderson K, Bailey S. Attributional style in depression: a meta-analytic review. *J Pers Soc Psychol*. 1986;50(5):974–991.
19. Teasdale JD, Scott J, Moore RG, et al. How does cognitive therapy prevent relapse in residual depression? evidence from a controlled trial. *J Consult Clin Psychol*. 2001;69(3):347–357.
20. Peterson TJ, Feldman G, Harley R, et al. Extreme response style in recurrent and chronically depressed patients: change with antidepressant administration and stability during continuation treatment. *J Consult Clin Psychol*. 2007;75(1):145–153.

21. Beevers CG, Keitner GI, Ryan CE, et al. Cognitive predictors of symptom return following depression treatment. *J Abnorm Psychol*. 2003;112(3): 488–496.
22. Johnson SL, Fingerhut R. Negative cognitive styles predict the course of bipolar depression, not mania. *J Cogn Psychother* 2004;18(2):149–162.
23. Reilly-Harrington NA, Alloy LB, Fresco DM, et al. Cognitive styles and life events interact to predict bipolar and unipolar symptomatology. *J Abnorm Psychol*. 1999;108(4):567–578.
24. Alloy LB, Reilly-Harrington N, Fresco DM, et al. Cognitive styles and life events in subsyndromal unipolar and bipolar disorders: stability and prospective prediction of depressive and hypomanic mood swings. *J Cogn Psychother*. 1999;13 (1):21–40.
25. Miklowitz DJ, Otto MW, Frank E, et al. Psychosocial treatments for bipolar depression: a 1-year randomized trial from the Systematic Treatment Enhancement Program. *Arch Gen Psychiatry*. 2007a;64(4):419–426.
26. Gitlin MJ, Swendsen J, Heller TL, et al. Relapse and impairment in bipolar disorder. *Am J Psychiatry*. 1995;152(11):1635–1640.
27. Harel EV, Levkovitz Y. Effectiveness and safety of adjunctive antidepressants in the treatment of bipolar depression: a review. *Isr J Psychiatry Relat Sci*. 2008;45(2):121–128.
28. Miklowitz DJ. Adjunctive psychotherapy for bipolar disorder: state of the evidence. *Am J Psychiatry*. 2008;165(11):1408–1419.
29. Lauder SD, Berk M, Castle DJ, et al. The role of psychotherapy in bipolar disorder. *Med J Aust*. 2010;193(suppl):S31–S35.
30. Cochran SD. Preventing medical noncompliance in the outpatient treatment of bipolar affective disorders. *J Consult Clin Psychol*. 1984;52(5):873–878.
31. Colom F, Vieta E, Sánchez-Moreno J, et al. Group psychoeducation for stabilised bipolar disorders: 5-year outcome of a randomised clinical trial. *Br J Psychiatry*. 2009;194(3):260–265.
32. Castle D, White C, Chamberlain J, et al. Group-based psychosocial intervention for bipolar disorder: randomised controlled trial. *Br J Psychiatry*. 2010;196(5):383–388.
33. Lam DH, Watkins ER, Hayward P, et al. A randomized controlled study of cognitive therapy for relapse prevention for bipolar affective disorder: outcome of the first year. *Arch Gen Psychiatry*. 2003;60(2):145–152.
34. Lam DH, Hayward P, Watkins ER, et al. Relapse prevention in patients with bipolar disorder: cognitive therapy outcome after 2 years. *Am J Psychiatry*. 2005;162(2):324–329.
35. Otto MW, Reilly-Harrington NA, Kogan JN, et al. *Managing Bipolar Disorder: A Cognitive-Behavioral Approach (Therapist Guide)*. New York, NY: Oxford University Press; 2009.
36. Sajatovic M, Davies M, Hrouda DR. Enhancement of treatment adherence among patients with bipolar disorder. *Psychiatr Serv*. 2004;55(3):264–269.
37. Scott J, Garland A, Moorhead S. A pilot study of cognitive therapy in bipolar disorders. *Psychol Med*. 2001;31(3):459–467.
38. Scott J, Paykel E, Morriss R, et al. Cognitive-behavioural therapy for severe and recurrent bipolar disorders: randomised controlled trial. *Br J Psychiatry*. 2006;188(4):313–320.
39. Miklowitz DJ, Simoneau TL, George EL, et al. Family-focused treatment of bipolar disorder: 1-year effects of a psychoeducational program in conjunction with pharmacotherapy. *Biol Psychiatry*. 2000;48(6):582–592.
40. Rea MM, Tompson MC, Miklowitz DJ, et al. Family-focused treatment versus individual treatment for bipolar disorder: results of a randomized clinical trial. *J Consult Clin Psychol*. 2003;71(3):482–492.
41. Frank E, Swartz HA, Kupfer DJ. Interpersonal and social rhythm therapy: managing the chaos of bipolar disorder. *Biol Psychiatry*. 2000;48(6):593–604.
42. Frank E, Kupfer DJ, Thase ME, et al. Two-year outcomes for interpersonal and social rhythm therapy in individuals with bipolar I disorder. *Arch Gen Psychiatry*. 2005;62(9):996–1004.
43. Sachs GS, Thase ME, Otto MW, et al. Rationale, design, and methods of the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD). *Biol Psychiatry*. 2003;53(11):1028–1042.
44. Miklowitz DJ, Otto MW, Frank E, et al. Intensive psychosocial intervention enhances functioning in patients with bipolar depression: results from a 9-month randomized controlled trial. *Am J Psychiatry*. 2007;164(9): 1340–1347.
45. Mitchell PB, Malhi GS. Bipolar depression: phenomenological overview and clinical characteristics. *Bipolar Disord*. 2004;6(6):530–539.
46. Sachs GS, Nierenberg AA, Calabrese JR, et al. Effectiveness of adjunctive antidepressant treatment for bipolar depression. *N Engl J Med*. 2007;356(17):1711–1722.
47. Gitlin M. Treatment-resistant bipolar disorder. *Mol Psychiatry*. 2006;11(3):227–240.
48. Treuer T, Tohen M. Predicting the course and outcome of bipolar disorder: a review. *Eur Psychiatry*. 2010;25(6):328–333.
49. Berk M, Parker G. The elephant on the couch: side-effects of psychotherapy. *Aust N Z J Psychiatry*. 2009;43(9):787–794.
50. Johnson SL. Life events in bipolar disorder: towards more specific models. *Clin Psychol Rev*. 2005;25(8):1008–1027.
51. Miklowitz DJ, Johnson SL. The psychopathology and treatment of bipolar disorder. *Annu Rev Clin Psychol*. 2006;2(1):199–235.
52. Peterson C, Semmel A, von Baeyer C, et al. The Attributional Style Questionnaire. *Cognit Ther Res*. 1982;6(3):287–299.
53. First MB, Spitzer RL, Gibbon M, et al. *Structured Clinical Interview for DSM-IV Axis I Disorders*. New York, NY: Biometrics Research Department, New York State Psychiatric Institute; 1995.
54. Sachs GS. Use of clonazepam for bipolar affective disorder. *J Clin Psychiatry*. 1990;51(suppl):31–34, discussion 50–53.
55. Sheehan DV, Lecrubier Y, Sheehan KH, et al. The Mini-International Neuropsychiatric Interview (MINI): the development and validation of a structured diagnostic psychiatric interview for *DSM-IV* and *ICD-10*. *J Clin Psychiatry*. 1998;59(suppl 20):22–33.
56. Otto MW, Reilly-Harrington NA, Knauz RO, et al. *Managing Bipolar Disorder: A Cognitive Behavior Treatment Program Workbook*. New York, NY: Oxford University Press; 2008.
57. Miklowitz DJ. *Bipolar Disorder: A Family-Focused Treatment Approach*. 2nd ed. New York, NY: Guilford Press; 2010.
58. Frank E. *Treating Bipolar Disorder: A Clinician's Guide to Interpersonal and Social Rhythm Therapy*. New York, NY: Guilford Press; 2005.
59. Sachs GS, Guille C, McMurrich SL. A clinical monitoring form for mood disorders. *Bipolar Disord*. 2002;4(5):323–327.
60. Otto MW, Simon NM, Wisniewski SR, et al; STEP-BD Investigators. Prospective 12-month course of bipolar disorder in out-patients with and without comorbid anxiety disorders.*Br J Psychiatry*. 2006;189:20-25.
61. Phillips ML, Travis MJ, Fagiolini A, et al. Medication effects in neuroimaging studies of bipolar disorder. *Am J Psychiatry*. 2008;165(3):313–320.
62. Reilly-Harrington NA, Miklowitz DJ, Otto MW, et al. Dysfunctional attitudes, attributional styles, and phase of illness in bipolar disorder. *Cognit Ther Res*. 2010;34(1):24–34.
63. Kraemer HC, Wilson GT, Fairburn CG, et al. Mediators and moderators of treatment effects in randomized clinical trials. *Arch Gen Psychiatry*. 2002;59(10):877–883.
64. Aiken LS, West SG. *Multiple Regression: Testing and Interpreting Interactions*. Newbury Park, CA: Sage; 1991.
65. Roberts JE, Gilboa E, Gotlib IH. Ruminative response style and vulnerability to episodes of dysphoria: gender, neuroticism and episode duration. *Cognit Ther Res*. 1998;22(4):401–423.
66. Mathews A, MacLeod C. Cognitive vulnerability to emotional disorders. *Annu Rev Clin Psychol*. 2005;1(1):167–195.
67. Jaeger J, Berns S, Loftus S, et al. Neurocognitive test performance predicts functional recovery from acute exacerbation leading to hospitalization in bipolar disorder. *Bipolar Disord*. 2007;9(1–2):93–102.
68. Teasdale JD, Moore RG, Hayhurst H, et al. Metacognitive awareness and prevention of relapse in depression: empirical evidence. *J Consult Clin Psychol*. 2002;70(2):275–287.
69. Williams JM, Alatiq Y, Crane C, et al. Mindfulness-Based Cognitive Therapy (MBCT) in bipolar disorder: preliminary evaluation of immediate effects on between-episode functioning. *J Affect Disord*. 2008;107(1–3):275–279.
70. Deckersbach T, Hölzel BK, Eisner LR, et al. Mindfulness-based cognitive therapy for nonremitted patients with bipolar disorder. *CNS Neurosci Ther*. 2012;18(2):133–141.
71. Miklowitz DJ, Alatiq Y, Goodwin GM, et al. A pilot study of mindfulness-based cognitive therapy for bipolar disorder. *Int J Cogn Ther*. 2009;2(4):373–382.
72. Alloy LB, Abramson LY, Walshaw PD, et al. Adolescent-onset bipolar spectrum disorders: a cognitive vulnerability-stress perspective. In: Miklowitz DJ, Cicchetti D, eds. *Understanding Bipolar Disorder: A Developmental Psychopathology Perspective*. New York, NY: Guilford Press; 2010:282–330.
73. Strakowski SM. Approaching the challenge of bipolar depression: results from STEP-BD. *Am J Psychiatry*. 2007;164(9):1301–1303.
74. Hankin BL, Fraley RC, Abela JR. Daily depression and cognitions about stress: evidence for a trait like depressogenic cognitive style and the prediction of depressive symptoms in a prospective daily diary study. *J Pers Soc Psychol*. 2005;88(4):673–685.
75. Deckersbach T, Nierenberg AA, Kessler R, et al. Cognitive rehabilitation for bipolar disorder: an open trial for employed patients with residual depressive symptoms. *CNS Neurosci Ther*. 2010;16(5):298–307.
76. Tabachnik BG, Fidell LS. *Using Multivariate Statistics*. 5th ed. Boston, MA: Pearson; 2007.